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<http://www.cas.org/support/stndgen/stndoc/properties.html>

=> s dalbavancin
L1 8 DALBAVANCIN

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=> s dalbavancin-protein
          8 DALBAVANCIN
          4755962 PROTEIN
L2          0 DALBAVANCIN-PROTEIN
          (DALBAVANCIN (W) PROTEIN)
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FILE LAST UPDATED: 30 Aug 2007 (20070830/ED)

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=> s l1
L3      95 L1

=> s l3 and albumen
      2727 ALBUMEN
L4      0 L3 AND ALBUMEN

=> s l3 and protein
      1994594 PROTEIN
L5      7 L3 AND PROTEIN

=> d 15 1-7

L5  ANSWER 1 OF 7  CA  COPYRIGHT 2007 ACS on STN
AN  147:133035  CA
TI  In vivo pharmacodynamic activity of the glycopeptide dalbavancin
AU  Andes, David; Craig, William A.
CS  Department of Medicine, University of Wisconsin, Madison, WI, 53792, USA
SO  Antimicrobial Agents and Chemotherapy (2007), 51(5), 1633-1642
     CODEN: AMACQ; ISSN: 0066-4804
PB  American Society for Microbiology
DT  Journal
LA  English
RE.CNT 33  THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
          ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5  ANSWER 2 OF 7  CA  COPYRIGHT 2007 ACS on STN
AN  146:38160  CA
TI  Dalbavancin: a novel lipoglycopeptide antibacterial
AU  Pope, Scott D.; Roecker, Andrew M.
CS  Department of Pharmacy, Carolinas Medical Center, Charlotte, NC, USA
SO  Pharmacotherapy (2006), 26(7), 908-918
     CODEN: PHPYDQ; ISSN: 0277-0008
PB  Pharmacotherapy Publications
DT  Journal; General Review
LA  English
RE.CNT 85  THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD
          ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5  ANSWER 3 OF 7  CA  COPYRIGHT 2007 ACS on STN
AN  142:370634  CA
TI  Differential inhibition of Staphylococcus aureus PBP2 by glycopeptide antibiotics
AU  Leimkuhler, Catherine; Chen, Lan; Barrett, Dianah; Panzone, Gianbattista; Sun, Binyuan; Falcone, Brian; Oberthuer, Markus; Donadio, Stefano; Walker, Suzanne; Kahne, Daniel
CS  Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA
SO  Journal of the American Chemical Society (2005), 127(10), 3250-3251
     CODEN: JACSAT; ISSN: 0002-7863
PB  American Chemical Society
```

DT Journal
LA English

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 7 CA COPYRIGHT 2007 ACS on STN
AN 141:28638 CA
TI Compositions and methods for treating bacterial infections with
protein-dalbavancin complexes
IN Cavaleri, Marco; Colombo, Luigi; Henkel, Timothy; Jabes, Daniela;
Malabarba, Adriano; Mosconi, Giorgio; Stogniew, Martin; White, Richard J.
PA Vicuron Pharmaceuticals Inc., USA
SO PCT Int. Appl., 90 pp.
CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004046196	A2	20040603	WO 2003-US36399	20031114
	WO 2004046196	A3	20040819		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003299561	A1	20040615	AU 2003-299561	20031114
	US 2005004011	A1	20050106	US 2003-713924	20031114
	US 2005130909	A1	20050616	US 2003-714166	20031114
	CN 1711102	A	20051221	CN 2003-80103406	20031114
	US 2005032721	A1	20050210	US 2004-942197	20040915
	US 2005130914	A1	20050616	US 2004-942604	20040915
PRAI	US 2002-427654P	P	20021118		
	US 2003-485694P	P	20030708		
	US 2003-495048P	P	20030813		
	US 2003-496483P	P	20030819		
	US 2003-714261	A1	20031114		
	WO 2003-US36399	W	20031114		
	US 2004-828483	A1	20040416		

L5 ANSWER 5 OF 7 CA COPYRIGHT 2007 ACS on STN
AN 140:369930 CA

TI Nonomuraea dbv gene cluster for biosynthesis of dalbavancin precursor,
antibiotic A40926
IN Donadio, Stefano; Sosio, Margherita; Beltrametti, Fabrizio
PA Vicuron Pharmaceuticals, Inc., USA
SO Eur. Pat. Appl., 165 pp.
CODEN: EPXXDW

DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1413626	A1	20040428	EP 2002-23597	20021023
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	CA 2501393	A1	20040506	CA 2003-2501393	20031015
	WO 2004038025	A2	20040506	WO 2003-EP11398	20031015
	WO 2004038025	A3	20040729		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
 GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
 LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
 OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
 TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2003294693 A1 20040513 AU 2003-294693 20031015
 EP 1578972 A2 20050928 EP 2003-785622 20031015
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 CN 1732263 A 20060208 CN 2003-80107411 20031015
 JP 2006516885 T 20060713 JP 2004-545854 20031015
 IN 2005DN01357 A 20070119 IN 2005-DN1357 20050404
 PRAI EP 2002-23597 A 20021023
 WO 2003-EP11398 W 20031015
 RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 7 CA COPYRIGHT 2007 ACS on STN
 AN 140:54179 CA
 TI The gene cluster for the biosynthesis of the glycopeptide antibiotic
 A40926 by *Nonomuraea* species
 AU Sosio, Margherita; Stinchi, Sofia; Beltrametti, Fabrizio; Lazzarini,
 Ameriga; Donadio, Stefano
 CS Vicuron Pharmaceuticals, Gerenzano, 21040, Italy
 SO Chemistry & Biology (2003), 10(6), 541-549
 CODEN: CBOLE2; ISSN: 1074-5521
 PB Cell Press
 DT Journal
 LA English
 RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 7 CA COPYRIGHT 2007 ACS on STN
 AN 135:254360 CA
 TI In vitro evaluation of BI 397, a novel glycopeptide antimicrobial agent
 AU Jones, R. N.; Biedenbach, D. J.; Johnson, D. M.; Pfaller, M. A.
 CS The Jones Microbiology Institute, North Liberty, IA, 52317, USA
 SO Journal of Chemotherapy (Firenze, Italy) (2001), 13(3), 244-254
 CODEN: JCHEEU; ISSN: 1120-009X
 PB E.I.F.T. srl
 DT Journal
 LA English
 RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 15 1-7 an ab

L5 ANSWER 1 OF 7 CA COPYRIGHT 2007 ACS on STN
 AN 147:133035 CA
 AB Dalbavancin is a lipoglycopeptide antibiotic with broad-spectrum activity
 against gram-pos. cocci and a markedly prolonged serum elimination
 half-life. We used the neutropenic murine thigh and lung infection models
 to characterize the pharmacodynamics of dalbavancin. Single-dose
 pharmacokinetic studies demonstrated linear kinetics and a prolonged
 elimination half-life which ranged from 7.6 to 13.1 h over the dose range
 of 2.5 to 80 mg/kg of body weight. The level of protein binding in
 mouse serum was 98.4%. The time course of in vivo activity of dalbavancin
 over the same dose range was examined in neutropenic ICR Swiss mice infected

with a strain of either *Streptococcus pneumoniae* or *Staphylococcus aureus* by using the thigh infection model. The burden of organisms for *S. pneumoniae* was markedly reduced over the initial 24 h of study, and organism regrowth was suppressed in a dose-dependent fashion for up to the entire 96 h of study following dalbavancin doses of 2.5 mg/kg or greater. Dalbavancin doses of 20 mg/kg or greater resulted in less killing of *S. aureus* but were still followed by a prolonged suppression of regrowth. Multiple-dosing-regimen studies with the same organisms were used to determine which of the pharmacodynamic indexes (maximum concentration in serum

[Cmax]/MIC,

area under the concentration-vs.-time curve [AUC]/MIC, or the duration of time that levels in serum exceed the MIC) best correlated with treatment efficacy. These studies used a dose range of 3.8 to 480 mg/kg/6 days fractionated into 2, 4, 6, or 12 doses over the 144-h dosing period. Nonlinear regression anal. was used to examine the data fit with each pharmacodynamic index. Dalbavancin administration by the use of large, widely spaced doses was the most efficacious for both organisms. Both the 24-h AUC/MIC and the Cmax/MIC parameters correlated well with the in vivo efficacy of treatment against *S. pneumoniae* and *S. aureus* (for 24-h AUC/MIC, $R^2 = 78$ and 77%, resp.; for Cmax/MIC, $R^2 = 90$ and 57%, resp.). The free-drug 24-h AUC/MICs required for a bacteriostatic effect were 17 ± 7 for five *S. pneumoniae* isolates. A similar treatment endpoint for the treatment against five strains of *S. aureus* required a larger dalbavancin exposure, with a mean free-drug 24-h AUC/MIC of 265 ± 143 . Beta-lactam resistance did not affect the pharmacodynamic target. The dose-response curves were relatively steep for both species; thus, the pharmacodynamic target needed to achieve organism redns. of 1 or 2 \log_{10} in the mice were not appreciably larger (1.3- to 1.6-fold). Treatment was similarly efficacious in neutropenic mice and in the lung infection model. The dose-dependent efficacy and prolonged elimination half-life of dalbavancin support the widely spaced regimens used in clin. trials. The free-drug 24-h AUC/MIC targets identified in these studies should be helpful for discerning rational susceptibility breakpoints. The current MIC90 for the target gram-pos. organisms would fall within this value.

L5 ANSWER 2 OF 7 CA COPYRIGHT 2007 ACS on STN
AN 146:38160 CA

AB A review. Dalbavancin is a new lipoglycopeptide antibacterial possessing in vitro activity against a variety of gram-pos. pathogens. Against methicillin-susceptible and methicillin-resistant *Staphylococcus aureus*, it has demonstrated favorable min. inhibitory concentration ranges compared

with

those of currently available agents. Dalbavancin is highly protein bound (> 90%), which may contribute to its prolonged half-life of 149-300 h. Because of this long half-life, once-weekly dosing strategies have been used in clin. trials. Efficacy and tolerability have been demonstrated in a wide variety of animal infection models. Clin. success and safety have been shown in phase II and III trials for skin and soft-tissue infections and a phase II trial for catheter-related bloodstream infections. In these trials with vancomycin, linezolid, and various β -lactams as comparators, comparable results have been reported. The results of further phase III trials are anxiously awaited and will more clearly define the clin. role of this novel agent.

L5 ANSWER 3 OF 7 CA COPYRIGHT 2007 ACS on STN
AN 142:370634 CA

AB Glycopeptide antibiotics prevent maturation of the bacterial cell wall by binding to the terminal D-alanyl-D-alanine moiety of peptidoglycan precursors, thereby inhibiting the enzymes involved in the final stages of peptidoglycan synthesis. However, there are significant differences in the biol. activity of particular glycopeptide derivs. that are not related to their affinity for D-Ala-D-Ala. The authors compare the ability of vancomycin and a set of clin. relevant glycopeptides to inhibit *Staphylococcus aureus* PBP2 (penicillin binding protein), the

major transglycosylase in a clin. relevant pathogen, *S. aureus*. They report expts. suggesting that activity differences between glycopeptides against this organism reflect a combination of substrate binding and secondary interactions with key enzymes involved in peptidoglycan synthesis.

L5 ANSWER 4 OF 7 CA COPYRIGHT 2007 ACS on STN
AN 141:28638 CA

AB The invention provides methods and compns. for treatment of bacterial infections. Methods of the invention include administration of dalbavancin for treatment of a bacterial infection, in particular a Gram-pos. bacterial infection of skin and soft tissue, under conditions where a protein-dalbavancin complex forms, or administering a protein-dalbavancin complex. Dosing regimes include once weekly administration of dalbavancin, which often remains at therapeutic levels in the bloodstream for at least one week, providing prolonged therapeutic action against a bacterial infection.

L5 ANSWER 5 OF 7 CA COPYRIGHT 2007 ACS on STN
AN 140:369930 CA

AB The present invention relates to the field of antibiotics and more specifically to the isolation of nucleic acid mols. that code for the biosynthetic pathway of the glycopeptide antibiotic A40926. Disclosed are the functions of the gene products involved in A40926 production. The present invention provides biosynthetic genes that code for A40926 production, the encoded polypeptides, the recombinant vectors comprising the nucleic acid sequences that encode said polypeptides, the host cells transformed with said vectors and methods for producing glycopeptide antibiotics using said transformed host cells, including methods for producing A40926, a precursor thereof, a derivative thereof or a modified glycopeptide different from A40926 or a precursor thereof.

L5 ANSWER 6 OF 7 CA COPYRIGHT 2007 ACS on STN
AN 140:54179 CA

AB The glycopeptide A40926 is the precursor of dalbavancin, a second-generation glycopeptide currently under clin. development. The dbv gene cluster, devoted to A40926 biosynthesis, was isolated and characterized from the actinomycete *Nonomuraea* species ATCC39727. From sequence anal., 37 open reading frames (ORFs) participate in A40926 biosynthesis, regulation, resistance, and export. Of these, 27 ORFs find a match in at least one of the previously characterized glycopeptide gene clusters, while 10 ORFs are, so far, unique to the dbv cluster. Putative genes could be identified responsible for some of the tailoring steps (attachment of glucosamine, sugar oxidation, and mannosylation) expected during A40926 biosynthesis. After constructing a *Nonomuraea* mutant by deleting ORFs 8 to 10, the novel compound dechloromannosyl-A40926 aglycon was isolated.

L5 ANSWER 7 OF 7 CA COPYRIGHT 2007 ACS on STN
AN 135:254360 CA

AB BI 397, a semi-synthetic amide derivative of the exptl. glycopeptide, MDL 62,476 (A40926), has excellent in vitro activity against a wide range of Gram-pos. organisms. In this extensive study, 630 contemporary (1998-2000) Gram-pos. isolates were selected from various resistance surveillance studies for their resistance patterns to fluoroquinolones, macrolides-lincosamides-streptogramins, β -lactams and glycopeptide agents. The BI 397 spectrum of activity was similar to that of other glycopeptides with a MIC₉₀ of ≤ 0.5 μ g/mL for all tested isolates with the exception of vancomycin-resistant enterococci Van A; (MIC₉₀, 32 μ g/mL). BI 397 was more potent than vancomycin and teicoplanin against *Staphylococcus aureus* (2- to 8-fold), β -hemolytic streptococci (equal to >16-fold), viridans group streptococci (equal to >32-fold), and *Corynebacterium* spp. including *C. jeikeium* (8- to >16-fold). BI 397 was also more active than quinupristin/dalfopristin against all Gram-pos.

organisms tested with the exception of oxacillin-susceptible *S. aureus*, against which it had equal activity. BI 397 has little activity against *Haemophilus influenzae* (MIC₉₀, 64 µg/mL) or other Gram-neg. bacilli (MIC₉₀, >64 µg/mL). BI 397 exhibited bacteriostatic activity (like the vancomycin control) vs. most species, but was bactericidal against tested *Streptococcus pneumoniae*. In vitro testing conditions with blood supplemented or free protein containing media elevated BI 397 MIC results, and the 30-µg disk seems acceptable for further disk diffusion test development. Animal pharmacokinetic data published elsewhere suggest that BI 397 may be dosed less frequently than teicoplanin and the results of early studies in humans are awaited with interest, especially when treating teicoplanin-refractory coagulase-neg. staphylococci.